

Amendments to the Specification and Abstract

In the Title:

Please amend the title to read as follows: --METHOD AND PREPARATION CONTAINING IDEBENONE FOR PROTECTING HUMAN SKIN--.

In the Specification:

Before the paragraph [0001], please delete the heading "Description" and insert new paragraph [0000.1] as follows:

--[0000.1] This application is a continuation of prior Application No. 10/030,842, filed January 9, 2002, which is hereby incorporated by reference herein.--.

Before paragraph [0006], please insert the heading --BACKGROUND--

Please replace paragraph [0014] with the following rewritten paragraph:

[0014] It has already been proposed to use vitamin E, a substance having known anti-oxidative action in sunscreen formulations, nevertheless even here the action achieved remains far below that hoped for. The production of pro-oxidative degradation products of tocopherol should thus be mentioned ~~in particular, which do not occur when using idebenone and/or its derivatives, or may be reliably intercepted when combining tocopherol and idebenone and/or its derivatives.~~

Before paragraph [0015] please insert the following new paragraph [0014.1]:

--[0014.1] Patent Documents DE 3 049 039, European 0 788 793 (13.8.1997), United States 4 436 753, United States 5 059 627, United States 5 916 925 and World 99 07 355 (see examples) indeed describe oral, parenteral or percutaneous preparations containing idebenone or its derivatives for the treatment of dementia, circulatory disturbances or for the induction of a neural growth factor. Patent document JP 1 279 818 describes the use of idebenone and its derivatives

in various preparations for colouring hair. Idebenone showed no toxic effects on oral administration (Barkworth et al., *Arzneim.-Forsch/Drug Res.* 35 (II), 11, pages 1704 ff. (1985)).--.

Please delete paragraph [0015], including Tables 1 through 3.

Please delete paragraph [0017].

Please replace paragraph [0018] with the following rewritten paragraph:

[0018] Light-sensitive skin includes photodermatoses. Further designations for the polymorphic light-dermatosis are PLD, PLE, Mallorca Acne and a plurality of further designations, as are given in the literature (for example A. Voelckel et al., *Zentralblatt Haut- und Geschlechtskrankheiten* (1989), 156, page2).

Before paragraph [0025] please insert the heading --SUMMARY OF THE INVENTION-- and paragraph [0024.1] as follows:

--[0024.1] It is an object of the present invention to provide cosmetic and dermatological preparations and sunscreen formulations, which serve for the prophylaxis and treatment of light-sensitive skin, in particular photodermatoses, preferably PLD.--.

Please replace paragraph [0025] with the following rewritten paragraph:

[0025] ~~One~~ It is also an object of the present invention ~~was~~ is to eliminate ~~the~~ disadvantages of the state of the art. In particular, active ingredients or preparations containing such active ingredients should be provided, which when used may reduce the damage to the skin by oxidative influence, if not completely prevent it and which additionally show a regenerating and vitalising effect on aging, stressed or damaged skin by supporting vesicular breathing, stabilisation of mitochondrial membranes and anti-apoptotic properties.

Before paragraph [0027] please insert new paragraphs [0026.1] - [0026.5] as follows

--[0026.1] The present invention also provides a method for reducing a skin change. The method includes: applying a topical preparation to the skin. The preparation includes an amount of an agent effective for reducing the skin change. The agent includes idebenone or a derivative of idebenone.

[0026.2] The present invention provides a method for protecting human skin against an oxidative process. The method includes applying a topical preparation to the skin. The preparation includes an amount of an agent effective for reducing an amount of oxidants or free-radicals in the skin. The agent includes idebenone or a derivative of idebenone.

[0026.3] Additionally, the present invention provides a method for stabilizing a cosmetic or dermatological preparation. The method includes providing in the preparation an amount of an agent effective for reducing an amount of oxidants or free-radicals in the preparation. The agent includes idebenone or a derivative of idebenone.

[0026.4] The present invention also provides a skin protection preparation. The preparation includes an ultraviolet filter substance and an amount of an agent effective for reducing a formation of oxidation products in human skin due to an oxidative process. The agent includes idebenone or a derivative of idebenone.

[0026.5] The present invention also provides a stabilized topical skin preparation. The preparation includes a first and an amount of an agent effective for reducing oxidants or free-radical degradation products of the first component. The agent includes idebenone or a derivative of idebenone. The first component may be vitamin A, a derivative of vitamin A, vitamin B, a derivative of vitamin B, vitamin C, a derivative of vitamin C, vitamin E, a derivative of vitamin C, hyaluronic acid and/or a derivative of hyaluronic acid.--.

Before paragraph [0028] please insert the heading --DETAILED DESCRIPTION-- and new paragraph [0027.1], including Tables 1 through 3, as follows:

--[0027.1] In separate pre-tests, idebenone was used in the macrophage LDL oxidation systems as anti-oxidant by way of comparison to alpha-tocopherol, ascorbic acid, coenzyme Q-10 and glutathione. This system is suitable for the simulation of cell-promoted oxidation of lipids induced by lipoxxygenase, such as for example occurs due to UV radiation. To determine the antioxidative effect of the individual substances, the amount of primary degradation products of lipid peroxidation, the lipid hydroperoxides, occurring in the course of time after 8 or 24 hours was determined by means of an HPLC chemiluminescence method (E. Wieland et al., Fresenius J. Anal. Chem., 343, 62-63 (1992)). In spite of considerably lower concentration of idebenone in the batch (10 μ moles/litre), a clearly stronger antioxidative effect was shown compared to ascorbic acid (50 μ moles/litre), alpha-tocopherol (100 μ moles/litre) and glutathione (50 μ moles/litre). This was shown in particular when combining the remaining anti-oxidants with tocopherol. Only idebenone was able here to reliably intercept the pro-oxidative effect of tocopherol oxidation products occurring after 24 hours (see Table 1). Ascorbic acid in particular, which is occasionally added in cosmetic and topical dermatological preparations already containing tocopherol, showed in this combination in the course of time only a significantly lower antioxidative effect. The values given in the following tables relate to nmoles of measured lipid hydroperoxides per mg of LDL protein.

Table 1

Oxidation system (reference values)

Time (hours)	Mk without additive	Mk + LDL (A)	A + 100 μmoles/litre - tocopherol (B)	LDL without additive
8	1.1	53.3	32.8	33.1
24	0	184.8	198.0	35.3

Table 2

Oxidation system (A) (+ 1 anti-oxidant)

Time (hours)	A + 100 μmoles/litre -tocopherol	A + 10 μmoles/litre idebenone	A + 50 μmoles/litre ascorbic acid	A + 50 μmoles/litre glutathione	A + 10 μmoles/litre coenzyme Q-10
8	32.8	0	0	51.7	69
24	198.0	0	1.7	119.0	115.8

Table 3

Oxidation system (B) (+ 1 further anti-oxidant)

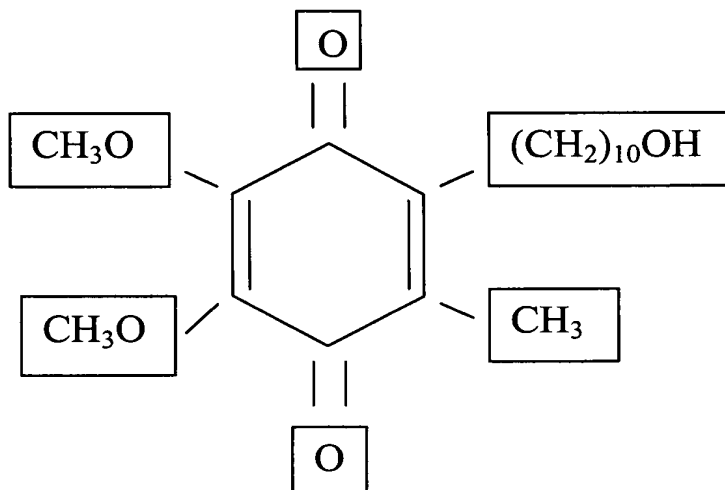
Time (hours)	B + 10 μmoles/litre idebenone	B + 50 μmoles/litre ascorbic acid	B + 50 μmoles/litre glutathione	B + 10 μmoles/litre coenzyme Q-10
8	1.9	1.7	23.3	26.8
24	2.6	25.3	129.8	143.7

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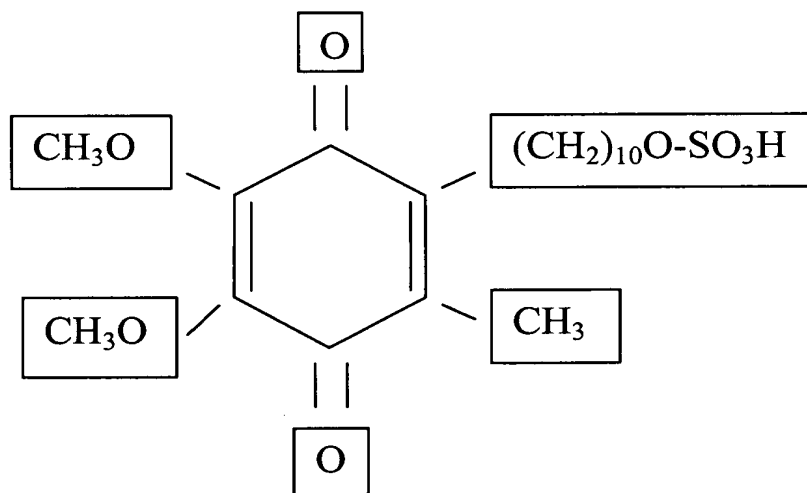
Please delete paragraphs [0028] and [0029].

Before paragraph [0030] please insert new paragraphs [0029.1] and [0029.2] as follows:

--[0029.1] Idebenone (6-(10-hydroxydecyl)-2,3-dimethoxy-5-methyl-1,4-benzoquinone) is characterized by the following structural formula:



[0029.2] An example of a hydrophilic idebenone ester (separate synthesis) is idebenone sulphonic acid, characterized by the following structural formula:



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Please delete paragraph [0031].

Before paragraph [0034] please insert new paragraph [0033.1] as follows:

--[0033.1] Pro-oxidative degradation products do not occur when using idebenone and/or its derivatives, or may be reliably intercepted when combining tocopherol and idebenone and/or its derivatives.--.

Please replace paragraph [0034] with the following rewritten paragraph:

[0034] The use of idebenone and/or its derivatives, such as for example idebenone sulphonic acid, is ~~therefore of the~~ within the scope of the present invention. The use of other derivatives of idebenone is of course also ~~of the~~ within the scope of the present invention.

Please replace paragraph [0035] with the following rewritten paragraph:

[0035] The use of idebenone and/or its derivatives as anti-oxidant and its use for combating and/or prophylaxis of skin aging caused by oxidative stress and inflammatory reactions are likewise ~~of the~~ within the scope of the present invention. The use of idebenone and/or its derivatives as anti-oxidants for the stabilisation of cosmetic or dermatological preparations, which contain as additive either vitamin A and/or its derivatives (for example all-E-retinoic acid, 9-Z-retinoic acid, 13-Z-retinoic acid, retinal, retinyl ester), vitamin B and/or its derivatives, vitamin C and/or its derivatives and vitamin E and/or its derivatives (for example alpha-tocopherol acetate) individually or in combination, is thus likewise ~~of the~~ within the scope of the present invention. The stabilising effect thus relates to both smell and colour and in particular to the active ingredient content of the preparation.

Please replace paragraph [0036] with the following rewritten paragraph:

[0036] Furthermore, the use of idebenone and its derivatives as an agent for supporting vesicular breathing and stabilisation of mitochondrial membranes with additional anti-apoptotic effect in skin cells and its use for the regeneration and revitalisation of aging, stressed or damaged skin, is therefore ~~also of the~~ within the scope of the present invention.

Please replace paragraph [0037] with the following rewritten paragraph:

[0037] The cosmetic or dermatological formulations of according to the present invention may be composed as is conventional and serve for the treatment, care and cleansing of the skin and as a make-up product in decorative cosmetics, for example. They preferably contain 0.0001 wt.% to 30 wt.%, preferably 0.05 wt.% to 5 wt.%, in particular 0.1-2.0 wt.%, based on the total weight of the agent, of idebenone and/or its derivatives.

Please replace paragraph [0049] with the following rewritten paragraph:

[0049] Emulsions ~~of the~~ according to the present invention are advantageous and contain, for example the said afore-mentioned fats, oils, waxes and other adipoids, and water and an emulsifier, as is used conventionally for such a type of formulation.

Please replace paragraph [0062] with the following rewritten paragraph:

[0062] Emulsions ~~of the~~ according to the present invention are advantageous and contain, for example the said afore-mentioned fats, oils, waxes and other adipoids, and water and an emulsifier, as is used conventionally for such a type of formulation.

Please replace paragraph [0063] with the following rewritten paragraph:

[0063] Gels according to the present invention conventionally contain alcohols of low C number, for example ethanol, isopropanol, 1,2-propane diol, glycerine and water or an above-mentioned oil in the presence of a thickening agent, which for oily-alcoholic gels is preferably silicon dioxide or an aluminium silicate, for aqueous-alcoholic or alcoholic gels is preferably a polyacrylate.

Please replace paragraph [0064] with the following rewritten paragraph:

[0064] The conventional known highly volatile, liquefied propellants, for example hydrocarbons (propane, butane, isobutane), which may be used alone or mixed with one another, are suitable as propellants for preparations which can be sprayed from aerosol containers according to the present invention. Compressed air can also advantageously be used.

Please replace paragraph [0065] with the following rewritten paragraph:

[0065] Preparations ~~of the~~ according to the present invention may also advantageously contain substances which absorb UV radiation in the UVB range, wherein the total quantity of filter substances is, for example 0.1 wt.% to 30 wt.%, preferably 0.5 to 10 wt.%, in particular 1.0 to 6.0 wt.%, based on the total weight of the preparations, in order to provide cosmetic preparations which protect the skin from the entire range of ultraviolet radiation. They may also serve as sunscreen agents for the skin.

Please replace paragraph [0066] with the following rewritten paragraph:

[0066] If the preparations ~~of the~~ according to the present invention contain UVB filter substances, they may be oil-soluble or water-soluble. According to the invention, advantageous oil-soluble UVB filters are, for example:

- mineral oils, mineral waxes;
- oils, such as triglycerides of capric or caprylic acid, also natural oils, such as for example castor oil;
- fats, waxes and other natural and synthetic adipoids, preferably esters of fatty acids with alcohols of low C number, for example with isopropanol, propylene glycol or glycerine, or esters of fatty alcohols with alkane acids of low C number or with fatty acids;
- alkyl benzoates;

- silicone oils, such as dimethylpolysiloxanes, diethylpolysiloxanes, diphenylpolysiloxanes and mixtures thereof.
- 3-benzylidene camphor derivatives, preferably 3-(4-methylbenzylidene) camphor, 3-benzylidene camphor;
- 4-aminobenzoic acid derivatives, preferably (2-ethylhexyl) 4-(dimethylamino) benzoate, amyl 4-(dimethylamino) benzoate;
- esters of cinnamic acid, preferably (2-ethylhexyl) 4-methoxycinnamate, isopentyl 4-methoxycinnamate;
- esters of salicylic acid, preferably (2-ethylhexyl) salicylate, (4-isopropyl-benzyl) salicylate, homomentyl salicylate,
- derivatives of benzophenone, preferably 2-hydroxy-4-methoxybenzophenone, 2-hydroxy-4-methoxy-4'-methylbenzophenone, 2,2'-dihydroxy-4-methoxybenzophenone;
- esters of benzylidenemalonic acid, preferably di(2-ethylhexyl) 4-methoxybenzylidenemalonate, - 2,4,6-trianilino(p-carbo-2'-ethyl-1'hexyloxy)-1,3,5-triazine.

Please replace paragraph [0068] with the following rewritten paragraph:

[0068] The list of the said UVB filters, which may be used in combination with the active ingredient combinations of the present invention, should of course not be limiting.

Please replace paragraph [0069] with the following rewritten paragraph:

[0069] ~~The object of the invention is also~~ Also within the scope of the present invention is the use of a combination of idebenone and/or its derivatives with at least one UVB filter as anti-oxidant or the use of a combination of idebenone and/or its derivatives with at least one UVB filter as anti-oxidant in a cosmetic or dermatological preparation.

Please replace paragraph [0071] with the following rewritten paragraph:

[0071] ~~The object of the invention is also~~ Also within the scope of the present invention is the use of a combination of idebenone and/or its derivatives with at least one UVA filter as anti-oxidant or the use of a combination of the active ingredient combinations of the invention with at least one UVA filter as anti-oxidant in a cosmetic or dermatological preparation.

Please replace paragraph [0072] with the following rewritten paragraph:

[0072] ~~The object of the invention is also~~ Also within the scope of the present invention is the use of a combination of idebenone and/or its derivatives with at least one UVA filter and at least one UVB filter as anti-oxidant or the use of a combination of idebenone and/or its derivatives with at least one UVA filter and at least one UVB filter as anti-oxidant in a cosmetic or dermatological preparation.

Please replace paragraph [0074] with the following rewritten paragraph:

[0074] These combinations of UVA filters and pigment or preparations containing this combination are also ~~an object of the invention within the scope of the present invention~~. The quantities mentioned for the above combinations may be used.

Please replace paragraph [0080] with the following rewritten paragraph:

[0080] The compositions ~~of the~~ according to the present invention contain, apart from the aforementioned surfactants, water and optionally the additives which are conventional in cosmetics, for example perfume, thickener, dyestuffs, deodorants, antimicrobial materials, back-fattening agents, complexing and sequestering agents, pearlescent agents, plant extracts, vitamins and/or their derivatives, active ingredients and the like.

Please replace paragraph [0084] with the following rewritten paragraph:

[0084] ~~The object of the invention is also the process~~ Also within the scope of the present invention are processes for producing the cosmetic agents of the invention, which is characterised in that active ingredient combinations of the invention are incorporated into cosmetic and dermatological formulations in a manner known per se.

Page 27, first line change "Patent claims" to --WHAT IS CLAIMED IS--.

In the Abstract:

Please replace the abstract of record with the following rewritten abstract:

~~The invention relates to the use of 6-(10-hydroxydecyl)-2,3-dimethoxy-5-methyl-1,4-benzochinol or its reduced form and/or the derivative thereof in regenerative and protective topical preparations.~~ A method for reducing a skin change includes applying an amount of idebenone (6-(10-hydroxydecyl)-2,3-dimethoxy-5-methyl-1,4-benzoquinone) or derivative of idebenone effective for reducing the skin change.